

contiguous amino acids. The new human Ras-like proteins and the polypeptides encoding them are useful in the diagnosis, prevention, and treatment of inflammation and disorders associated with cell proliferation and apoptosis. They are also useful in treating AIDS and other infectious or genetic immunodeficiencies, neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, cerebellar degeneration), aplastic anemia, ischemic injuries (myocardial infarction, stroke), toxin-induced diseases (alcohol-induced liver damage, cirrhosis, lathyrism), cachexia, viral infections (hepatitis B and C), cancer and osteoporosis. The nucleic acid molecules are useful as probes, primers and chemical intermediates in biological assays, for constructing recombinant vectors, expressing antigenic portions of the protein. The peptide and nucleic acid sequences are useful as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate kinase activity in cells and tissues that express the kinase. The host cells are useful in producing a kinase protein or peptide, and non-human transgenic animals. This sequence represents the human Ras-like protein of the invention

Sequence 615 AA;

Query Match 100.0%; Score 3226; DB 5; Length 615;
Best Local Similarity 100.0%; Pred. No. 2.3e-282;
Matches 615; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

1 MAGTLDLGGCTVEELRGCTIEAFDPSGKVPOLVRIFLMMHPYIPSSQLAKLHIY 60
1 MAGTLDLGGCTVEELRGCTIEAFDPSGKVPOLVRIFLMMHPYIPSSQLAKLHIY 60
61 QOSRKDNNSLSQVKTCHLVRYWISAPPAFDLNPDLAEQIKELKALLDQGNRRHSLID 120
61 QOSRKDNNSLSQVKTCHLVRYWISAPPAFDLNPDLAEQIKELKALLDQGNRRHSLID 120
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
181 FVTHGCTVDNPNVLERISLFNSVSQWVQMLISKPTAPQALVTHFVAAEKLQLONF 240
181 FVTHGCTVDNPNVLERISLFNSVSQWVQMLISKPTAPQALVTHFVAAEKLQLONF 240
181 FVTHGCTVDNPNVLERISLFNSVSQWVQMLISKPTAPQALVTHFVAAEKLQLONF 240
241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKLMGTELVATNGYNGYRRRLAACVGR 300
241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKLMGTELVATNGYNGYRRRLAACVGR 300
241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKLMGTELVATNGYNGYRRRLAACVGR 300
301 FPIIGVHLKQIVLQALPMDLPARTLNKAKKOLFSILBELAMVTSILAPVQANPDL 360
301 FPIIGVHLKQIVLQALPMDLPARTLNKAKKOLFSILBELAMVTSILAPVQANPDL 360
301 FPIIGVHLKQIVLQALPMDLPARTLNKAKKOLFSILBELAMVTSILAPVQANPDL 360
361 LSLLTSLDQVOTDELYQLSLOREPRSKSPTSPSTCTPPRPVLEMTSAKPKLDQ 420
361 LSLLTSLDQVOTDELYQLSLOREPRSKSPTSPSTCTPPRPVLEMTSAKPKLDQ 420
421 ALVVEHEIKWVESVFRFDFVDGDGHIISGEFQIIRGNFPYLSAFGDLDQDQGISREEM 480
421 ALVVEHEIKWVESVFRFDFVDGDGHIISGEFQIIRGNFPYLSAFGDLDQDQGISREEM 480
481 VSYFLRSSSVLGGMGVTFHNFQESNSILPVAQCHCKALLIGIYQGLKCRACGVNCHKQC 540
481 VSYFLRSSSVLGGMGVTFHNFQESNSILPVAQCHCKALLIGIYQGLKCRACGVNCHKQC 540
541 KDRLSVCRRRAQSVLSGSAFSPSPMSHHRAPSPSLPRGRGRSPPALIPAPATRE 600
541 KDRLSVCRRRAQSVLSGSAFSPSPMSHHRAPSPSLPRGRGRSPPALIPAPATRE 600
601 BEVQTEDEGVFDIHL 615
601 BEVQTEDEGVFDIHL 615

AAW87995
ID AAW87995 standard; protein; 609 AA.

AAW87995;

15-APR-1999 (first entry)

An alternatively spliced human MCG7 protein.

MCG4 protein; gene regulatory function; heat shock protein;

quantine nucleotide exchange factor protein; MCG7 protein;

heat shock-binding protein; MCG18 protein; zinc finger protein; cancer.

Homo sapiens.

MO9853061.A1.

26-NOV-1998.

22-MAY-1998; 98WO-AU000380.

23-MAY-1997; 97AU-00006972.

23-MAY-1997; 97AU-00006973.

22-JAN-1998; 98AU-00001458.

22-JAN-1998; 98AU-00001459.

22-JAN-1998; 98AU-00001460.

(COUNCIL QUEENSLAND INST MEDICAL RES.

Hayward N, Silins G, Grimmond S, Gartside M, Hancock J;

WPI; 1999-070146/06.

N-PSDB; AAX04553.

New gene-expression regulatory genes, mcg4, mcg7, and mcg18 - encode a zinc finger protein, a GEF, and a heat shock or heat shock binding protein, useful to detect and treat cancer.

Claim 5; Fig 13b; 80pp; English.

The present sequence represents a MCG7 protein. The protein has gene regulatory functions, and has homology to a heat shock protein or heat shock-binding protein. The specification also describes MCG4, which is homologous to guanine nucleotide exchange factor protein, and MCG18, which is homologous to a zinc finger protein. Detection of mutations in the MCG genes can be used to identify the propensity for various types of cancer, and to treat, arrest, or otherwise ameliorate, the effects of a cancer in an animal or bird

Sequence 609 AA;

Query Match 98.6%; Score 3180; DB 2; Length 609;
Best Local Similarity 98.9%; Pred. No. 3.3e-278;
Matches 608; Conservative 1; Mismatches 0; Indels 6; Gaps 1;

1 MAGTLDLGGCTVEELRGCTIEAFDPSGKVPOLVRIFLMMHPYIPSSQLAKLHIY 60
1 MAGTLDLGGCTVEELRGCTIEAFDPSGKVPOLVRIFLMMHPYIPSSQLAKLHIY 60
61 QOSRKDNNSLSQVKTCHLVRYWISAPPAFDLNPDLAEQIKELKALLDQGNRRHSLID 120
61 QOSRKDNNSLSQVKTCHLVRYWISAPPAFDLNPDLAEQIKELKALLDQGNRRHSLID 120
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
121 IDSVPTTKRKQVOTQNPVGOKKRMKSLFDHLEPMELAEHLTYLEYSFCKILFODYHS 180
181 FVTHGCTVDNPNVLERISLFNSVSQWVQMLISKPTAPQALVTHFVAAEKLQLONF 240
181 FVTHGCTVDNPNVLERISLFNSVSQWVQMLISKPTAPQALVTHFVAAEKLQLONF 240
241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKLMGTELVATNGYNGYRRRLAACVGR 300
241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKLMGTELVATNGYNGYRRRLAACVGR 300

Exhibit A

DB 241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKMEGLTELVATNGYNGYRRRLAACVGR 300

QY 301 PPIIGVHLKDLVALQALPMDLPARTRLNGAKMKQLFSEBELAMVTSLRPPVQAMPDL 360

DB 301 PPIIGVHLKDLVALQALPMDLPARTRLNGAKMKQLFSEBELAMVTSLRPPVQAMPDL 360

QY 361 LSLITVSLDQYQTEDELYQLSLQREPRKSSPTSPSCPTPPRPVLEWTSAAKPKLDQ 420

DB 361 LSLITVSLDQYQTEDELYQLSLQREPRKSSPTSPSCPTPPRPVLEWTSAAKPKLDQ 420

QY 421 ALVVEHIEKRVESVFRNPDVDGSHISQREFOIIRGNFPYLSAFGLDQNDGCTISREEM 480

DB 421 ALVVEHIEKRVESVFRNPDVDGSHISQREFOIIRGNFPYLSAFGLDQNDGCTISREEM 480

QY 481 VSYFLRSSSVLGGRMGVNHPQESNSLRPVACRCKALILGIYKQGLKCRACGVNCHKQC 540

DB 481 VSYFLRSSSVLGGRMGVNHPQESNSLRPVACRCKALILGIYKQGLKCRACGVNCHKQC 540

QY 541 KDRLSVECRRAQSVSLSGSAPSPSPMHSRRAFSFSLPRGRGRSPPALPLPAETIRE 600

DB 541 KDRLSVECRRAQSVSLSGSAPSPSPMHSRRAFSFSLPRGRGRSPPALPLPAETIRE 600

QY 601 EEVQTEDEGVFDIHL 615

DB 595 EEVQTEDEGVFDIHL 609

RESULT 3
AAY70961
ID AAY70961 standard; protein; 609 AA.

XX AAY70961;
AC AAY70961;
XX 09-AUG-2000 (first entry)

DE Human Ras signalling pathway associated protein CalDAG-GEFI.

XX Human Ras signalling pathway associated protein CalDAG-GEFI.
XX Human, Ras signalling pathway; CalDAG-GEFI; calcium; DAG; diacylglycerol;
KM GEF; guanine nucleotide exchange factor; Rap1A; diagnosis; treatment;
KM CalDAG-GEF-associated disorder; drug; transgenic animal model;
XX Ras-associated cancer; protein therapy.

OS Homo sapiens.
XX
XX Key
FH Location/Qualifiers
FT 150..173
FT /label= SCRI
FT /note= "Structurally conserved region which is highly
FT homologous to Ras/superfamily GSPs"
FT 220..262
FT /label= SCRI
FT /note= "Structurally conserved region which is highly
FT homologous to Ras-superfamily GSPs"
FT 299..320
FT /label= SCRI
FT /note= "Structurally conserved region which is highly
FT homologous to Ras-superfamily GSPs"
FT 433..452
FT /label= EF-hand
FT /note= "calcium binding motif"
FT 499..548
FT /label= DAG/phorbol ester-binding domain
FT /note= "present in most protein Kinase C family members"

PN W0200024768-A2.
XX
XX 04-MAY-2000.
XX
XX 22-OCT-1999; 89WO-US024826.
XX
XX 23-OCT-1998; 98US-010507P.
PR 16-NOV-1998; 98US-0106685P.

XX (MAST) MASSACHUSETTS INST TECHNOLOGY.
PA Kawasaki H, Graybiel A, Houseman D;
XX WPI; 2000-350690/30.
XX N-PSDB; AAD00311.
XX Isolated nucleic acid comprises nucleotide sequence encoding protein
XX selected from normal or mutant CalDAG-guanine nucleotide exchange factor.
XX
XX Claim 64; Page 90-92; 128pp; English.

CC The present sequence is a CalDAG-guanine nucleotide exchange factor
CC (GEFI) from a human frontal cortex and U937 lambdaZAP library.
CC The CalDAG-GEFI has substrate specificity for Rap1A, dual binding domains
CC for calcium and diacylglycerol (DAG) and highly expressed in brain,
CC particularly in brain basal ganglia pathways and their axon-terminal
CC regions. Expression of CalDAG-GEFI activates Rap1A and inhibits Ras-
CC dependent activation of the extracellular-signal-regulated kinase/mitogen
CC -activated protein (ERK/MAP) kinase cascade in 293T cells. The CalDAG-GEF
CC proteins play an important role in determining the relative activation of
CC Ras and Rap1 signalling induced by calcium and DAG mobilisation in brain
CC and haematopoietic organs. The present sequence is used for diagnosis and
CC treatment (by protein therapy) of CalDAG-GEF-associated disorders. It is
CC also useful for developing drugs and producing cell-lines or transgenic
CC animal models for Ras-associated cancers

XX
XX Sequence 609 AA;
SQ

Query Match 98.6%; Score 3180; DB 3; Length 609;
Best Local Similarity 98.9%; Pred. No. 3.3e-278;
Matches 608; Conservative 1; Mismatches 0; Indels 6; Gaps 1;

QY 1 MAGTLDLDCGCTVEELRGCEIAEYDSGKVRDPOLVRIFLMMHWPYIPSSQLAAKLHIY 60

DB 1 MAGTLDLDCGCTVEELRGCEIAEYDSGKVRDPOLVRIFLMMHWPYIPSSQLAAKLHIY 60

QY 61 QOSRKNNSLSLOVTKCHLVWTSAPPAEFDINBELAQIKELKALLDQSGNRHSLID 120

DB 61 QOSRKNNSLSLOVTKCHLVWTSAPPAEFDINBELAQIKELKALLDQSGNRHSLID 120

QY 121 IDSVPTKMKROYTORPVQOKKXKSLFDHLEPMLEHLYLTYLXRSFCKIIFQDVHS 180

DB 121 IDSVPTKMKROYTORPVQOKKXKSLFDHLEPMLEHLYLTYLXRSFCKIIFQDVHS 180

QY 181 FVTHGCTVNDPVLRFSLSNSVSQVQMLISKPTAPQALVTHFEVHAKLLQLONF 240

DB 181 FVTHGCTVNDPVLRFSLSNSVSQVQMLISKPTAPQALVTHFEVHAKLLQLONF 240

QY 241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKMEGLTELVATNGYNGYRRRLAACVGR 300

DB 241 NTLMVAVGSLSHSSISRLKETHSHVSPETIKMEGLTELVATNGYNGYRRRLAACVGR 300

QY 301 PPIIGVHLKDLVALQALPMDLPARTRLNGAKMKQLFSEBELAMVTSLRPPVQAMPDL 360

DB 301 PPIIGVHLKDLVALQALPMDLPARTRLNGAKMKQLFSEBELAMVTSLRPPVQAMPDL 360

QY 361 LSLITVSLDQYQTEDELYQLSLQREPRKSSPTSPSCPTPPRPVLEWTSAAKPKLDQ 420

DB 361 LSLITVSLDQYQTEDELYQLSLQREPRKSSPTSPSCPTPPRPVLEWTSAAKPKLDQ 420

QY 421 ALVVEHIEKRVESVFRNPDVDGSHISQREFOIIRGNFPYLSAFGLDQNDGCTISREEM 480

DB 421 ALVVEHIEKRVESVFRNPDVDGSHISQREFOIIRGNFPYLSAFGLDQNDGCTISREEM 480

QY 481 VSYFLRSSSVLGGRMGVNHPQESNSLRPVACRCKALILGIYKQGLKCRACGVNCHKQC 540

DB 481 VSYFLRSSSVLGGRMGVNHPQESNSLRPVACRCKALILGIYKQGLKCRACGVNCHKQC 540

QY 541 KDRLSVECRRAQSVSLSGSAPSPSPMHSRRAFSFSLPRGRGRSPPALPLPAETIRE 600

DB 541 KDRLSVECRRAQSVSLSGSAPSPSPMHSRRAFSFSLPRGRGRSPPALPLPAETIRE 600